=> d bib,ab 1-13

L5 ANSWER 1 OF 13 CAPLUS COPYRIGHT 2003 ACS
AN 2003:508929 CAPLUS
TI Molecular mechanisms of hereditary neuropathy : genotype-phenotype correlation
AU Nakagawa, Masanori; Takashima, Hiroshi
CS Department of Neurology, Research Institute for Neurological and Geriatrics, Kyoto Prefectural University of Medicine, Kyoto, 602-0841, Japan
SO Rinsho Byori (2003), 51(6), 536-543
CODEN: RBYOAI; ISSN: 0047-1860
PB Nippon Rinsho Kensa Igakkai
DT Journal
LA Japanese
AB Hereditary neuropathies are classified into several subtypes according to clin., electrophysiol. and pathol. findings. Recent genetic studies have revealed their phenotypic and genetic diversities. In the primary peripheral demyelinating neuropathies (CMT1), at least 9 genes have been assocd. with the disorders; altered dosage of peripheral **myelin** protein 22 (PMP22) or point **mutation** of PMP22, the gap junction protein 1 (GJB1), the **myelin** protein zero gene (MPZ), the early growth response gene 2 (EGR2), the myotubularin-related protein 2 gene (MTMR2), the N-myc downstream-regulated gene 1 (NDRG1), the L-**periaxin** gene (PRX), SRY-related HMG-BOX gene 10 (SOX10) and the ganglioside-induced differentiation-assocd. protein 1 gene (GDAP1). In the primary peripheral axonal neuropathies (CMT2), at least 8 genes have been assocd. with these disorders; the neurofilament light chain gene (NEFL), the kinesin 1B gene (KIF1B), the gigaxonin gene (GAN1), Lamin A/C (LMNA) and tyrosyl-DNA phosphodiesterase 1 (TDP1). In addn., some **mutations** in GJB1, MPZ and GDAP1 also present with clin. and electrophysiol. findings of CMT2. **Mutation** of NEFL or KIF1B cause dominantly inherited axonal neuropathies, whereas **mutation** of GJB1 or MPZ can present as genocopies of dominant axonal neuropathies. In addn., to the above diseases, we have reported a new type of NMSNP (MIM # *604484) characterized by proximal dominant neurogenic atrophy, obvious sensory nerve involvement and the locus on 3q13. Here, we summarize the genetic bases of hereditary neuropathies and attempt to highlight significant genotype-phenotype correlations.

L5 ANSWER 2 OF 13 CAPLUS COPYRIGHT 2003 ACS
AN 2003:233055 CAPLUS
DN 138:335248
TI Molecular mechanisms of hereditary neuropathy: genotype-phenotype correlation
AU Nakagawa, Masanori
CS Department of Neurology, Research Institute for Neurological Diseases and Geriatrics, Kyoto Prefectural University of Medicine, Japan
SO Kyoto-furitsu Ika Daigaku Zasshi (2003), 112(2), 81-90
CODEN: KFIZAO; ISSN: 0023-6012
PB Kyoto-fu Igaku Shinkokai
DT Journal; General Review
LA Japanese
AB A review. Hereditary neuropathies are classified into several subtypes according to clin., electrophysiol. and pathol. findings. Recent genetic studies have revealed their phenotypic and genetic diversities. In the primary peripheral demyelinating neuropathies (CMT1), at least 9 genes have been assocd. with the disorders; altered dosage of peripheral **myelin** protein 22 (PMP22) or point **mutation** of PMP22, the gap junction protein 1 (GJB1), the **myelin** protein zero gene (MPZ), the early growth response gene 2 (EGR2), the myotubularin-related protein 2 gene (MTMR2), the N-myc downstream-regulated gene 1 (NDRG1), the L-**periaxin** gene (PRX), SRY-related HMG-BOX gene 10 (SOX10) and

the ganglioside-induced differentiation-assocd. protein 1 gene (GDAP1). In the primary peripheral axonal neuropathies (CMT2), at least 8 genes have been assocd. with these disorders; the neurofilament light chain gene (NEFL), the kinesin 1B gene (K1FIB), the gigaxonin gene (GAN1), Lamin A/C (LMNA) and tyrosyl-DNA phosphodiesterase 1 (TDP1). In addn., some **mutations** in GJB1, MPZ and GDAP1 also present with clin. and electrophysiol. findings of CMT2. **Mutation** of NEFL or KIF1B cause dominantly inherited axonal neuropathies, whereas **mutation** of GJB1 or MPZ can present as genocopies of dominant axonal neuropathies. In addn. to the above diseases, we have reported a new type of HMSNP (MIM #*604484) characterized by proximal dominant neurogenic atrophy, obvious sensory nerve involvement and the gene locus on 3q13. Here, we summarize the genetic bases of hereditary neuropathies and attempt to highlight significant genotype-phenotype correlations.

L5 ANSWER 3 OF 13 CAPLUS COPYRIGHT 2003 ACS
AN 2002:504902 CAPLUS
DN 137:77308
TI Defects in **periaxin** associated with **myelinopathies** leads to diagnostic and drug screening applications
IN Lupski, James R.; Boerkoel, Cornelius F.; Takashima, Hiroshi
PA Baylor College of Medecine, USA
SO PCT Int. Appl., 99 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

	PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI	WO 2002051981	A2	20020704	WO 2001-US48935	20011213
	W: CA, JP				
	US 2003039987	A1	20030227	US 2001-21955	20011213
PRAI	US 2000-255217P	P	20001213		

AB The present invention is based on the discovery that **mutational** defects in the **periaxin** (PRX) gene and/or protein are assocd. with **myelinopathies**, including Charcot-Marie-Tooth syndrome and/or Dejerine-Sottas syndrome. Unrelated individuals having a **myelinopathy** from Dejerine-Sottas syndrome have recessive PRX **mutations**. The PRX locus maps to a region assocd. with a severe autosomal recessive demyelinating neuropathy and is also syntenic to the Prx location on murine chromosome 7. Numerous specific **mutations** in the gene and protein are provided. These defects provide applications for diagnostic tests (e.g. by PCR, sequencing, hybridization, DHPLC), screening for therapeutic agents, and gene therapy.

L5 ANSWER 4 OF 13 MEDLINE DUPLICATE 1
AN 2002361060 MEDLINE
DN 22104999 PubMed ID: 12112076
TI **Periaxin mutations** cause a broad spectrum of demyelinating neuropathies.
AU Takashima Hiroshi; Boerkoel Cornelius F; De Jonghe Peter; Ceuterick Chantal; Martin Jean-Jacques; Voit Thomas; Schroder J-Michael; Williams Anna; Brophy Peter J; Timmerman Vincent; Lupski James R
CS Department of Molecular and Human Genetics, Baylor College of Medicine, One Baylor Plaza, Houston, TX 77030, USA.
NC K08 DK 02738 (NIDDK)
R01 NS 27042 (NINDS)
SO ANNALS OF NEUROLOGY, (2002 Jun) 51 (6) 709-15.
Journal code: 7707449. ISSN: 0364-5134.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200208

ED Entered STN: 20020712
Last Updated on STN: 20020810
Entered Medline: 20020809

AB Previous studies have demonstrated that apparent loss-of-function **mutations** in the **periaxin** gene cause autosomal recessive Dejerine-Sottas neuropathy or severe demyelinating Charcot-Marie-Tooth disease. In this report, we extend the associated phenotypes with the identification of two **additional** families with novel **periaxin** gene **mutations** (C715X and R82fsX96) and provide detailed neuropathology. Each patient had marked sensory involvement; two siblings with a homozygous C715X **mutation** had much worse sensory impairment than motor impairment. Despite early disease onset, these siblings with the C715X **mutation** had relatively slow disease progression and adult motor impairment typical of classic demyelinating Charcot-Marie-Tooth neuropathy. In contrast, a patient with the homozygous R82fsX96 **mutation** had a disease course consistent with Dejerine-Sottas neuropathy. The neuropathology of patients in both families was remarkable for demyelination, onion bulb and occasional tomacula formation with focal **myelin** thickening, abnormalities of the paranodal **myelin** loops, and focal absence of paranodal septate-like junctions between the terminal loops and axon. Our study indicates a prominent sensory neuropathy resulting from **periaxin** gene **mutations** and suggests a role for the carboxyl terminal domain of the **periaxin** protein.

L5 ANSWER 5 OF 13 MEDLINE DUPLICATE 2
AN 2002660462 MEDLINE
DN 22278714 PubMed ID: 12390521
TI Antibodies to L-**periaxin** in sera of patients with peripheral neuropathy produce experimental sensory nerve conduction deficits.
AU Lawlor Mike W; Richards Michael P; De Vries George H; Fisher Morris A; Stubbs Evan B Jr
CS Neurology and Research Services, Department of Veterans Affairs, Neurology Service (127)Building 1, Edward Hines Jr Hospital, Hines, IL 60141, USA.
SO JOURNAL OF NEUROCHEMISTRY, (2002 Nov) 83 (3) 592-600.
Journal code: 2985190R. ISSN: 0022-3042.
CY England: United Kingdom
DT (CLINICAL TRIAL)
(CONTROLLED CLINICAL TRIAL)
Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200211
ED Entered STN: 20021108
Last Updated on STN: 20021214
Entered Medline: 20021126

AB L-**Periaxin** is a PDZ-domain protein localized to the plasma membrane of **myelinating** Schwann cells and plays a key role in the stabilization of mature **myelin** in peripheral nerves. **Mutations** in L-**periaxin** have recently been described in some patients with demyelinating peripheral neuropathy, suggesting that disruption of L-**periaxin** function may result in nerve injury. In this study, we report the presence of autoantibodies to L-**periaxin** in sera from two of 12 patients with diabetes mellitus (type 2)-associated neuropathy and three of 17 patients with IgG monoclonal gammopathy of undetermined significance (MGUS) neuropathy, an autoimmune peripheral nerve disorder. By comparison, anti-L-**periaxin** antibodies were not present in sera from nine patients with IgM MGUS neuropathy or in sera from 10 healthy control subjects. The effect of anti-L-**periaxin** serum antibody on peripheral nerve function was tested in vivo by intraneural injection. Sera containing anti-L-**periaxin** antibody, but not sera from age-matched control subjects, injected into the endoneurium of rat sciatic nerve significantly ($p < 0.005$, $n = 3$) attenuated sensory-evoked compound muscle action

potential (CMAP) amplitudes in the absence of temporal dispersion. In contrast, motor-evoked CMAP amplitudes and latencies were not affected by intraneural injection of sera containing anti-L-**periaxin** antibody. Light and electron microscopy of anti-L-**periaxin** serum-injected nerves showed morphologic evidence of demyelination and axon enlargement. Depleting sera of anti-L-**periaxin** antibodies neutralized the serum-mediated effects on nerve function and nerve morphology. Together, these data support anti-L-**periaxin** antibody as the pathologic agent in these serum samples. We suggest that anti-L-**periaxin** antibodies, when present in sera of patients with IgG MGUS- or diabetes-associated peripheral neuropathy, may elicit sensory nerve conduction deficits.

L5 ANSWER 6 OF 13 MEDLINE DUPLICATE 3
AN 2002347638 MEDLINE
DN 22084765 PubMed ID: 12090399
TI The function of the **Periaxin** gene during nerve repair in a model of CMT4F.
AU Williams Anna C; Brophy Peter J
CS Department of Preclinical Veterinary Sciences, University of Edinburgh, Summerhall, UK.
SO JOURNAL OF ANATOMY, (2002 Apr) 200 (4) 323-30. Ref: 24
Journal code: 0137162. ISSN: 0021-8782.
CY England: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 200207
ED Entered STN: 20020702
Last Updated on STN: 20020720
Entered Medline: 20020719
AB **Mutations** in the **Periaxin** (PRX) gene are known to cause autosomal recessive demyelinating Charcot-Marie-Tooth (CMT4F) and Dejerine-Sottas disease. The pathogenesis of these diseases is not fully understood. However, progress is being made by studying both the **periaxin**-null mouse, a mouse model of the disease, and the protein-protein interactions of **periaxin**. L-**periaxin** is a constituent of the dystroglycan-dystrophin-related protein-2 complex linking the Schwann cell cytoskeleton to the extracellular matrix. Although **periaxin**-null mice **myelinate** normally, they develop a demyelinating peripheral neuropathy later in life. This suggests that **periaxin** is required for the stable maintenance of a normal **myelin** sheath. We carried out sciatic nerve crushes in 6-week-old **periaxin**-null mice, and, 6 weeks later, found that although the number of **myelinated** axons had returned to normal, the axon diameters remained smaller than in the contralateral uncrushed nerve. Not only do **periaxin**-null mice have more hyper-**myelinated** axons than their wild-type counterparts but they also recapitulate this hypermyelination during regeneration. Therefore, **periaxin**-null mice can undergo peripheral nerve remyelination, but the regulation of peripheral **myelin** thickness is disrupted.

L5 ANSWER 7 OF 13 MEDLINE
AN 2002473493 IN-PROCESS
DN 22220850 PubMed ID: 12235586
TI [Clinical aspects and diagnostic and therapeutic approaches to motor and sensory hereditary neuropathies (NHMS)].
Aspectos clinicos y abordaje diagnostico y terapeutico de las neuropatias hereditarias sensitivomotoras.
AU Colomer Oferil J
CS Hospital Sant Joan de Deu, Esplugues de Llobregat, Espa a.
SO REVISTA DE NEUROLOGIA, (2002 Aug 1) 35 (3) 239-45.

Journal code: 7706841. ISSN: 0210-0010.
CY Spain
DT Journal; Article; (JOURNAL ARTICLE)
LA Spanish
FS IN-PROCESS; NONINDEXED; Priority Journals
ED Entered STN: 20020918
Last Updated on STN: 20021213
AB INTRODUCTION. The classifications of peripheral neuropathies are continually being revised in the light of advances in genetic and biochemical investigation. OBJECTIVE. We establish a classification based on the pathology found in different anatomical structures of nerves: the Schwann cell, **myelin**, axon and the different genes involved in causing neuropathies. Diagnosis is based on data from the clinical history, physical examination and electromyography and their correlation with the type of inheritance in relation to the different genes localized to (a) the Schwann cell: **periaxin** gene (PRX) encoding L and S **periaxin**. Stabilisation of the **myelin** acting as a signal tranducer. NDRG1 down stream regulated gene 1 and 2 acting as transcription factors in embryogenesis. EGR2/Krox 20 has an important function in **myelinization**. (b) **Myelin**: P0 membrane protein zero (MPZ) stabilizes the **myelin**. P1 **myelin** basic protein (MBP), is analogous to the **myelin** protein of the central nervous system (CNS) P2 found in the cytoplasm. PMP22 (peripheral **myelin** protein) also stabilizes the protein. MAG (**myelin** associated glycoprotein) has antigenic properties. (c). Axon. A foundational **mutation** (892C Y) in the gene of the lamina (LMNA) of the light neurofilaments (NF L). **Mutations** in the KIF1Bb gene which encodes the protein kinesin. We also make an aetiological analysis of some classical syndromes, especially the D jerine Sottas syndrome. CONCLUSION. The systematization used, based on clinical and electrophysiological data in relation to the different genes involved in the various anatomical structures constitutes a logical, diagnostic approach which is very useful.

L5 ANSWER 8 OF 13 MEDLINE DUPLICATE 4
AN 2002103532 MEDLINE
DN 21823270 PubMed ID: 11835375
TI Charcot-Marie-Tooth disease and related neuropathies: **mutation** distribution and genotype-phenotype correlation.
AU Boerkoel Cornelius F; Takashima Hiroshi; Garcia Carlos A; Olney Richard K; Johnson John; Berry Katherine; Russo Paul; Kennedy Shelley; Teebi Ahmad S; Scavina Mena; Williams Lowell L; Mancias Pedro; Butler Ian J; Krajewski Karen; Shy Michael; Lupski James R
CS Department of Molecular and Human Genetics, Baylor College of Medicine, Houston, TX, USA.
NC K08 DK02738 (NIDDK)
R01 NS27042 (NINDS)
SO ANNALS OF NEUROLOGY, (2002 Feb) 51 (2) 190-201.
Journal code: 7707449. ISSN: 0364-5134.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200203
ED Entered STN: 20020209
Last Updated on STN: 20030222
Entered Medline: 20020301
AB Charcot-Marie-Tooth disease (CMT) is a genetically heterogeneous disorder that has been associated with alterations of several proteins: peripheral **myelin** protein 22, **myelin** protein zero, connexin 32, early growth response factor 2, **periaxin**, myotubularin related protein 2, N-myc downstream regulated gene 1 product, neurofilament light chain, and kinesin 1B. To determine the frequency of **mutations** in these genes among patients with CMT or a related peripheral neuropathy,

we identified 153 unrelated patients who enrolled prior to the availability of clinical testing, 79 had a 17p12 duplication (CMT1A duplication), 11 a connexin 32 **mutation**, 5 a **myelin** protein zero **mutation**, 5 a peripheral **myelin** protein 22 **mutation**, 1 an early growth response factor 2 **mutation**, 1 a **periaxin mutation**, 0 a myotubularin related protein 2 **mutation**, 1 a neurofilament light chain **mutation**, and 50 had no identifiable **mutation**; the N-myc downstream regulated gene 1 and the kinesin 1B gene were not screened for **mutations**. In the process of screening the above cohort of patients as well as other patients for CMT-causative **mutations**, we identified several previously unreported mutant alleles: two for connexin 32, three for **myelin** protein zero, and two for peripheral **myelin** protein 22. The peripheral **myelin** protein 22 **mutation** W28R was associated with CMT1 and profound deafness. One patient with a CMT2 clinical phenotype had three **myelin** protein zero **mutations** (I89N+V92M+I162M). Because one-third of the **mutations** we report arose de novo and thereby caused chronic sporadic neuropathy, we conclude that molecular diagnosis is a necessary adjunct for clinical diagnosis and management of inherited and sporadic neuropathy.

L5 ANSWER 9 OF 13 MEDLINE
AN 2002351777 MEDLINE
DN 22089829 PubMed ID: 12094560
TI Neuropathology of some hereditary conditions affecting central and peripheral nervous system.
AU Martin J J; Ceuterick C
CS Born-Bunge Foundation, University of Antwerp.. jjmneuro@uia.ua.ac.be
SO ACTA NEUROLOGICA BELGICA, (2002 Mar) 102 (1) 30-5. Ref: 23
Journal code: 0247035. ISSN: 0300-9009.
CY Belgium
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LA English
FS Priority Journals
EM 200212
ED Entered STN: 20020704
Last Updated on STN: 20021219
Entered Medline: 20021218
AB Neuropathology plays a crucial role in the phenotypic individualization of hereditary disorders affecting the central and peripheral nervous system even if molecular genetics represents the most essential step in describing the genotypes. The neuropathological description of phenotypes and genotypes can be used for refining clinical skills and understanding many clinical, neurophysiological and neuroradiological features. It contributes to the diagnosis of such disorders. The use of immunohistochemical techniques in combination with molecular genetics improves also our knowledge of their pathogenesis and might participate to the future development of therapeutic strategies. We discuss new features of spino-cerebellar ataxia (SCA) type 7 and of a recently identified SCA17 in order to illustrate the significance of the neuronal intranuclear inclusions (NIIs) described in various CAG/polyglutamine repeat expansion diseases. In the field of the peripheral neuropathies we present data on a newly described autosomal recessive Charcot-Marie-Tooth disease (CMT4F) with **mutations** in the **periaxin** gene. We document a dysjunction between **myelin** loops and axolemma with disappearance of the septate-like junctions or transverse bands. The significance of this dysjunction is not yet elucidated. We hope to show by these examples that the combination of classical and new neuropathological methods is useful in the study of hereditary disorders of the nervous system.

L5 ANSWER 10 OF 13 MEDLINE DUPLICATE 5

AN 2002205623 MEDLINE
DN 21936408 PubMed ID: 11939347
TI Recent progress on the molecular organization of **myelinated** axons.
AU Scherer Steven S; Arroyo Edgardo J
CS Department of Neurology, The University of Pennsylvania Medical Center, Philadelphia 19104, USA.. sscherer@mail.med.upenn.edu
NC NS08075 (NINDS)
NS34528 (NINDS)
NS37100 (NINDS)
SO JOURNAL OF THE PERIPHERAL NERVOUS SYSTEM, (2002 Mar) 7 (1) 1-12.
Journal code: 9704532. ISSN: 1085-9489.
CY United States
DT (LECTURES)
LA English
FS Priority Journals
EM 200210
ED Entered STN: 20020410
Last Updated on STN: 20021008
Entered Medline: 20021004
AB The structure of **myelinated** axons was well described 100 years ago by Ramon y Cajal, and now their molecular organization is being revealed. The basal lamina of **myelinating** Schwann cells contains laminin-2, and their abaxonal/outer membrane contains two laminin-2 receptors, alpha6beta4 integrin and dystroglycan. Dystroglycan binds utrophin, a short dystrophin isoform (Dp116), and dystroglycan-related protein 2 (DRP2), all of which are part of a macromolecular complex. Utrophin is linked to the actin cytoskeleton, and DRP2 binds to **periaxin**, a PDZ domain protein associated with the cell membrane. Non-compact **myelin**--found at incisures and paranodes--contains adherens junctions, tight junctions, and gap junctions. Nodal microvilli contain F-actin, ERM proteins, and cell adhesion molecules that may govern the clustering of voltage-gated Na+ channels in the nodal axolemma. Na(v)1.6 is the predominant voltage-gated Na+ channel in mature nerves, and is linked to the spectrin cytoskeleton by ankyrinG. The paranodal glial loops contain neurofascin 155, which likely interacts with heterodimers composed of contactin and Caspr/paranodin to form septate-like junctions. The juxtaparanodal axonal membrane contains the potassium channels Kv1.1 and Kv1.2, their associated beta2 subunit, as well as Caspr2. Kv1.1, Kv1.2, and Caspr2 all have PDZ binding sites and likely interact with the same PDZ binding protein. Like Caspr, Caspr2 has a band 4.1 binding domain, and both Caspr and Caspr2 probably bind to the band 4.1 B isoform that is specifically found associated with the paranodal and juxtaparanodal axolemma. When the paranode is disrupted by **mutations** (in cgt-, contactin-, and Caspr-null mice), the localization of these paranodal and juxtaparanodal proteins is altered: Kv1.1, Kv1.2, and Caspr2 are juxtaposed to the nodal axolemma, and this reorganization is associated with altered conduction of **myelinated** fibers. Understanding how axon-Schwann interactions create the molecular architecture of **myelinated** axons is fundamental and almost certainly involved in the pathogenesis of peripheral neuropathies.

L5 ANSWER 11 OF 13 MEDLINE DUPLICATE 6
AN 2001322321 MEDLINE
DN 21096917 PubMed ID: 11157804
TI A **mutation** in **periaxin** is responsible for CMT4F, an autosomal recessive form of Charcot-Marie-Tooth disease.
AU Guilbot A; Williams A; Ravise N; Verny C; Brice A; Sherman D L; Brophy P J; LeGuern E; Delague V; Bareil C; Megarbane A; Claustres M
CS INSERM U289, Hopital de la Salpetriere, 47 Boulevard de l'Hopital, Paris, France.. guilbot@ccr.jussieu.fr
SO HUMAN MOLECULAR GENETICS, (2001 Feb 15) 10 (4) 415-21.
Journal code: 9208958. ISSN: 0964-6906.

CY England: United Kingdom
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
EM 200106
ED Entered STN: 20010611
Last Updated on STN: 20010611
Entered Medline: 20010607
AB Charcot-Marie-Tooth (CMT) disease is a heterogeneous group of inherited peripheral motor and sensory neuropathies characterized by chronic distal weakness with progressive muscular atrophy and sensory loss in the distal extremities. Inheritance can be autosomal dominant, X-linked or autosomal recessive (ARCMT). Recently, a locus responsible for a demyelinating form of ARCMT disease, named CMT4F, has been mapped on 19q13 in a large consanguineous Lebanese family. L- and S-**periaxin** are proteins of **myelinating** Schwann cells and homozygous **periaxin** -null mice display extensive demyelination of **myelinated** fibers in the peripheral nervous system, which suggests that the **periaxin** gene is a good candidate gene for an ARCMT disease. The human gene encoding the periaxins (PRX) was mapped to 19q13, in the CMT4F candidate interval. After characterizing the human PRX gene, we identified a nonsense R196X **mutation** in the Lebanese family which cosegregated with CMT. Histopathological and immunohistochemical analysis of a sural nerve biopsy of one patient revealed common features with the mouse mutant and the absence of L-**periaxin** from the **myelin** sheath. These data confirm the importance of the **periaxin** proteins to normal Schwann cell function and substantiate the utility of the **periaxin**-null mouse as a model of ARCMT disease.

L5 ANSWER 12 OF 13 CAPLUS COPYRIGHT 2003 ACS
AN 2001:413140 CAPLUS
DN 135:150846
TI EGR2 **mutations** in inherited neuropathies dominant-negatively inhibit **myelin** gene expression
AU Nagarajan, Rakesh; Svaren, John; Le, Nam; Araki, Toshiyuki; Watson, Mark; Milbrandt, Jeffrey
CS Departments of Pathology and Internal Medicine, Washington University School of Medicine, St. Louis, MO, 63110, USA
SO Neuron (2001), 30(2), 355-368
CODEN: NERNET; ISSN: 0896-6273
PB Cell Press
DT Journal
LA English
AB The identification of EGR2 **mutations** in patients with neuropathies and the phenotype Egr2/Krox20-/- have demonstrated that the Egr2 transcription factor is crit. for peripheral nerve **myelination**. However, the mechanism by which these **mutations** cause disease remains unclear, as most patients present with disease in the heterozygous state, whereas Egr2+/- mice are phenotypically normal. To understand the effect of aberrant Egr2 activity on Schwann cell gene expression, we performed microarray expression profiling to identify genes regulated by Egr2 in Schwann cells. These include genes encoding **myelin** proteins and enzymes required for synthesis of normal **myelin** lipids. Using these newly identified targets, we have shown that neuropathy-assocd. EGR2 mutants dominant-neg. inhibit wild-type Egr2-mediated expression of essential **myelin** genes to levels sufficiently low to result in the abnormal **myelination** obsd. in these patients.
RE.CNT 68 THERE ARE 68 CITED REFERENCES AVAILABLE FOR THIS RECORD
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 13 OF 13 MEDLINE DUPLICATE 7
AN 2001143341 MEDLINE

DN 21090499 PubMed ID: 11133365
TI **Periaxin mutations** cause recessive Dejerine-Sottas neuropathy.
CM Erratum in: Am J Hum Genet 2001 Feb;68(2):557
AU Boerkoel C F; Takashima H; Stankiewicz P; Garcia C A; Leber S M; Rhee-Morris L; Lupski J R
CS Department of Molecular and Human Genetics, Baylor College of Medicine, Houston, TX 77030, USA.
NC K08 DK02738 (NIDDK)
R01 NS27042 (NINDS)
SO AMERICAN JOURNAL OF HUMAN GENETICS, (2001 Feb) 68 (2) 325-33. Journal code: 0370475. ISSN: 0002-9297.
CY United States
DT Journal; Article; (JOURNAL ARTICLE)
LA English
FS Priority Journals
OS GENBANK-AF321191; GENBANK-AF321192; GENBANK-118200; GENBANK-145900; GENBANK-162500; GENBANK-605253; OMIM
EM 200103
ED Entered STN: 20010404
Last Updated on STN: 20030105
Entered Medline: 20010308
AB The **periaxin** gene (PRX) encodes two PDZ-domain proteins, L- and S-**periaxin**, that are required for maintenance of peripheral nerve **myelin**. Prx(-/-) mice develop a severe demyelinating peripheral neuropathy, despite apparently normal initial formation of **myelin** sheaths. We hypothesized that **mutations** in PRX could cause human peripheral **myelinopathies**. In accordance with this, we identified three unrelated Dejerine-Sottas neuropathy patients with recessive PRX **mutations**-two with compound heterozygous nonsense and frameshift **mutations**, and one with a homozygous frameshift **mutation**. We mapped PRX to 19q13.13-13.2, a region recently associated with a severe autosomal recessive demyelinating neuropathy in a Lebanese family (Delague et al. 2000) and syntenic to the location of Prx on murine chromosome 7 (Gillespie et al. 1997).